directed to non-statutory subject matter. The Examiner has further rejected Claims 1-4 under 35 U.S.C. §102(b) or, alternatively, under 35 U.S.C. §103 as describing subject matter which is allegedly anticipated by, or obvious over, the publications by Masuno, et al. entitled "Interaction of Monoclonal Antibodies with Cell Surface Antigens of Human Ovarian Carcinomas," Cancer Res., Vol. 44, pp. 2813-2819 (March 30, 1984) ("Masuno, et al.") or Bast, et al. entitled "A Radioimmunoassay using a Monoclonal Antibody to Monitor the Course of Epithelial Ovarian Cancer," N. Engl. J. Med., Vol. 309, No. 15, pp. 883-887 (1983) ("Bast, et al."). The Examiner has also rejected Claims 5-10 under 35 U.S.C. §103 as allegedly being unpatentable over Masuno, et al. and Bast, et al., supra, in view of either U. S. Patent No. 4,623,621 to Pestka (1986) ("Pestka") or PCT Application No. WO 85/00663.

In response to the objections, the Applicant has amended the Abstract of the Disclosure and the Specification, both of which are considered to overcome the Examiner's objections. Specifically, the Applicant has amended the Abstract of the Disclosure to fully comply with the requirements of 37 C.F.R. §1.72(b) and has amended the Specification to correctly identify the author intended.

In response to the rejections, the Applicant has amended the claims, which when considered with the comments herein, are deemed to place the present case in condition for allowance. Specifically, the Applicant has cancelled Claim 2 without prejudice and has amended Claims 1, 3, 5, 6, and 7. Favorable reconsideration of Claims 1 and 2-10 is, therefore, respectfully requested.

In response to the Examiner's rejection of Claims 1-4 (Claim 2 having been cancelled) under 35 U.S.C. §112, first paragraph, the Applicant has amended the claims to specifically

recite that the antigen is "associated with ovarian tumors." Support for this recitation is found at Page 6, Lines 12-15, of the Specification. Accordingly, the Examiner's rejection under 35 U.S.C. §112, first paragraph, is overcome and withdrawal thereof is respectfully requested.

With respect to the Examiner's rejection of Claims 1-10 (Claim 2 presently cancelled) under 35 U.S.C. §112, second paragraph, the Applicant has amended Claims 1, 3, 5, 6, and 7 to specifically recite that CA125 is "ovarian tumor associated." Such an expression appears, as above, in the Specification at Page 6, Line 12-15. Claims 1, 3, 5, 6, and 7, as amended, are deemed to be sufficiently definite to satisfy the statutory requirement. Claim 4 depends from and contains all the limitations of amended Claim 3; similarly, Claims 8, 9, and 10 all depend from amended Claim 7 and contain all the limitations therein. Each of these claims is, therefore, sufficently definite, in turn, to satisfy the statute in this regard.

The Examiner further alleges that the recitation of the phrase "time sufficient" renders the method taught in Claim 6 vague and indefinite as regards, for example, the time required to form a binary complex. The Applicant respectfully submits that the Examiner's position is unwarranted as a matter of practicing the invention of Claim 6. Just as other various parameters and requirements of the invention are readily appreciated by one skilled in the art, the actual techniques used in forming the binary and ternary complexes of Claim 6 are left to the acquired knowledge of the practioner's skill, as is the amount of time needed. It is the contention of the Applicant that the amount of "time sufficient" to form the complex(es) of Claim 6 is not vague or indefinite: it is a

condition reasonably within the knowledge of those skilled in the art to which this patent application is addressed and is supported by the Specification, e.g., at Pages 12 and 23, Lines 11-13 and 9-19, respectively. Claims are read in light of the Specification and the level of the skilled artisan. See, e.g., W. L. Gore & Associates, Inc. V. Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983); alternatively, the "time sufficient" can be readily determined without resort to undue experimentation. See, In re Angstadt, 537 F.2d 498, 190 U.S.P.Q. 214 (CCPA 1976). Further in this regard, the Examiner is referred to the Specification, Page 12, Lines 11-14. The Examiner's rejection under 35 U.S.C. §112, second paragraph, has, therefore, been overcome and withdrawal thereof is respectfully requested.

In an effort to further delineate the claimed invention and in order to eliminate any ambiguity which may have been present heretofore, the Applicant has amended Claim 1 (Claim 2 having been canceled) to recite the term "an isolated, substantially purified" subunit of CA125. Support for this feature can be found, for example, at Page 7, Lines 18-24 of the Specification. Accordingly, the Examiner's rejection under 35 U.S.C. §101 is obviated and withdrawal thereof is respectfully requested.

In support of the rejections of Claims 1-4 under 35 U.S.C. §§102(b) and 103, the Examiner has cited the references to Masuno, et al. and Bast, et al. The Examiner alleges that Masuno, et al. disclose a monoclonal antibody specific to distinct determinants on the surface of human ovarian cancer cells and that Bast, et al. disclose a monoclonal antibody which recognizes the antigen CA125. The Examiner further alleges that this is the same antigen of the present invention. Claims 1-4 (Claim 2 presently canceled), as amended, relate to a subunit of ovarian tumor associated CA125 and the

complementary antibodies which have specificity for this 40 kilodalton subunit. This claimed 40 kilodalton subunit is uniquely associated with ovarian cancer and neither the subunit itself nor the corresponding antibody is taught or suggested by either Masuno, et al. or Bast, et al.

The law is settled that in order to "anticipate" a claimed invention under 35 U.S.C. §102(b), a single prior art reference must disclose each and every element of the claimed invention. Structural Rubber Products Co. V. Park Rubber Co., 749 F.2d 707, 715-716; 223 U.S.P.Q. 1264, 1270 (Fed. Cir. 1984). Both Masuno, et al. and Bast, et al. fail to disclose a subunit of CA125 having a molecular weight of about 40 kilodaltons. Consequently, as a matter of law, the Examiner's rejection under 35 U.S.C. §102(b) is overcome and withdrawal is respectfully requested.

The Masuno, et al. and Bast, et al. references are also cited by the Examiner in rejecting Claims 1-4 on the alternate ground of 35 U.S.C. §103. In this regard, the Examiner's attention is directed to Page 5, Lines 1-18 of the Specification, where the Applicant discusses both of the cited references. In brief, the references teach the use of a monoclonal antibody and an antigen--namely, CA125--in efforts to monitor ovarian cancer. However, these prior art attempts at diagnosis and tracking were complicated by the fact that CA125, as such, is present not only in ovarian cancer but also in: 1. benign diseases, such as endometriosis and pelvic inflammation; 2. normal developmental processes, such as in the amniotic fluid during gestation; and finally, 3. in normal cells (in this regard, the Examiner is directed to Pages 5 and 6 of the Specification, Lines 18-32 and 1-20, respectively). The problem solved by the present invention, therefore, is not how to detect

CA125 antigen with a monoclonal antibody, but rather how to reduce or eliminate the interference from those levels of CA125 which are produced by non-ovarian tumors and normal tissue in order that one may specifically detect ovarian cancer. The Applicant submits that one seeking a solution to this problem would hardly be disposed, on any objective basis, to consider references like Masuno, et al. or Bast, et al., neither of which is concerned with the reduction or removal of cross-reactivity.

The present invention, Claims 1-4, as amended, relate to the discovery of a unique subunit contained in the CA125 antigen that is specifically associated with ovarian cancer. The utilization of this heretofore unknown subunit reduces and eliminates the cross-reactions generated by those levels of CA125 antigen not associated with ovarian cancer. The Examiner avers that the "specific determinants and antibody of Masuno, et al. inherently have the same characteristics as required by the claims" (emphasis supplied). The Applicant submits that the antigen subunit and corresponding antibody described by Claims 1-4, as amended, do not have the "same characteristics" as taught by Masuno, et al.

By way of example, the Examiner is referred to the Specification, Page 6, Lines 15-16, wherein it is stated that normal tissue, when tested, does not show the presence of the claimed subunit of the CA125 molecule. Clearly, when the claimed subunit is detected in ovarian cancer and not in normal tissue, as is the antigen described in the references cited by the Examiner, one cannot speak of them as having the "same characteristics." Furthermore, the claimed subunit of ovarian tumor-associated CA125 is not "identical", as alleged by the Examiner, with CA125 proper: CA125 is found in a variety of conditions, both normal and non-ovarian, whereas the subunit is

unique to ovarian cancer. The Examiner's allegation that the CA125 antigen, as a whole, would inherently possess the claimed subunit as part of its make-up is submitted by the applicant to be an improper basis for an obviousness rejection under 35 U.S.C. §103; inherency and obviousness are distinct concepts. W. L. Gore, 721 F.2d 1540,200 USPQ 303. Even assuming, pro arguendo, that the antigen CA125 does embody the specific subunit of the present invention, the references cited by the Examiner do not teach or even remotely suggest the use of that particular subunit to specifically diagnose ovarian cancer. While the cross-reactivity problem solved by the present invention is alluded to in the prior art (see, for example, Bast, et al. Page 883, Column 2, Lines 5-8 where it is stated that CA125, such as it is, has been assayed in healthy patients, benign diseases and nongynecological malignant diseases, as well as ovarian cancer), the cited art does not convey the solution contemplated by the present discovery as embodied in the instant claims. Finally, as a matter of unexpected or superior results, the Applicant submits that the subunit and complementary antibody of Claims 1-4 are entitled to patent protection in that each exhibit substantially greater diagnostic accuracy for ovarian cancer than that shown by the prior art. Simply stated, the present discovery overcomes the long standing limitation of the prior art. The Examiner's rejection of Claims 1-4 under 35 U.S.C. §103 is deemed to have been overcome and withdrawal thereof is respectfully requested.

In support of the rejection of Claims 5-10 under 35 U.S.C. §103, the Examiner has cited the publications to Masuno, et al. and Bast, et al. in view of either U. S. Patent No. 4,623,621 to Pestka or the WO 85/00663. The Examiner alleges that Pestka and the WO Patent disclose a two-site or sandwich assay employing polyclonal and monoclonal antibodies. In

response, the Applicant has amended Claims 5, 6, and 7 to recite that the antigen is specifically associated with ovarian tumors. Support for this recitation is found at Page 6, Lines 12-15 of the Specification. Claims 8, 9, and 10, in turn, depend from and recite all the limitations of amended Claim 7. The Applicant submits that the preceding comments and remarks with respect to Masuno, et al. and Bast, et al., along with the present amendments to Claims 5, 6, and 7, are sufficient to overcome the rejection of Claims 5-10 under 35 U.S.C. §103 and withdrawal is, therefore, respectfully requested.

The Examiner has cited U. S. Patent No. 4,666,845 to Mattes, et al. and U. S. Patent No. 4,713,351 to Knauf as being made of record but not relied upon. The Applicant has considered these references, but they are not pertinent to the claims.

The Examiner has requested Applicant's assistance in obtaining a copy of Knaaf and Urback, Am. J. Obstet. Gynecol. 138: 1222, 1980 cited on Page 4, Lines 21-23 of the Specification. While a copy of this reference is unavailable as of the date of this Amendment, the Applicant will forward the same to the Examiner with all due speed.

Thus, in view of the foregoing Amendments and Remarks, it is respectfully requested that the present case be forwarded to allowance.

Respectfully submitted,

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